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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,408	08/10/2001	Volker Gerdts	9000-0058	6385

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,408	GERDTS ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/30/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The restriction/election requirement mailed October 15, 2003 is withdrawn. Claims 1-25 are examined in this office action.

Please note that the examiner and art unit assignment has been changed. The examiner now is Deborah Crouch, Ph.D., Art Unit 1632. The examiner's phone number and other contacting information are in the final paragraph of this office action.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-25 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-6, 8-14 and 16-27 of copending Application No. 10/155,867. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 7-12 and 14-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5, 7, 13 and 15 of copending Application No. 10/155,867. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are generic to the claims of '867.

Claims 1-5, 7-12 and 14-25 are to methods of eliciting an immune response comprising administering a vaccine composition comprising nucleic acid molecule encoding a selected antigen to a subject in utero, mucosally or orally via the amniotic fluid. Claims 7 and 15 of '867 are to methods of eliciting an immune response comprising administering a vaccine composition comprising nucleic acid molecule encoding a hepatitis virus antigen to a subject in utero, mucosally or orally via the amniotic fluid. The present specification defines "selected antigen" as including a hepatitis virus antigen. Thus, at the time of the present invention, it would have been obvious to the ordinary artisan to reach the invention of claims 7 and 15 of '867 given present claims 1-5, 7-12 and 14-25.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of eliciting an immune response in

fetal sheep in utero during the third trimester a first vaccine composition comprising plasmid vector comprising a nucleic acid molecule encoding a herpesvirus antigenoperably linked to a promoter, wherein expression of the nucleic acid sequence results in the newborn sheep exhibiting protection against challenge, and methods of eliciting an immune response in sheep comprising administering directly to a mucosal membrane or directly into the mouth of a fetal sheep in utero during the third trimester a first vaccine composition comprising a plasmid vector comprising a nucleic acid molecule encoding a herpes virus antigen operably linked to a promoter and administering the first vaccine composition a second time to the sheep at birth or a subunit herpesvirus or hepatitis virus vaccine to the sheep at birth, wherein expression of the nucleic acid sequence results in the newborn sheep exhibiting protection against challenge, does not reasonably provide enablement for the breath of any antigen, delivery in utero, oral delivery via the amniotic fluid in utero or any time during fetal development for delivery, or without achieving protection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-25 as presently written do not have an enabled use, as the specification does not provide guidance for merely producing an immune response with is not protective. The specification is replete with the need to vaccinate prior to birth to protect newborn animals, with particular emphasis on traditional livestock, from devastating infectious diseases that cause frequent death in new born animals (see specification, page 1-6). It is not evident from the present disclosure how the skilled artisan could use an immune response that is not protective.

In addition, claims 1-25 are not enabled for the breadth of "under conditions that permit the expression of said antigen" as the only guidance provided for expression is

expression is through operable linkage of the antigen nucleic acid sequence to a promoter. Neither the specification nor any art available teach a means to cause expression of the nucleic acid sequence other than through a promoter or expression regulatory sequence.

Claims 1-25 are not enabled because at the time of filing the art taught that the induction of a protective immune response through the administration of a nucleic acid sequence encoding an antigen was unpredictable. The claims are drawn to both the administration of the nucleic acid via a plasmid vector alone or through some other vector means such as a viral vector or complexed with a liposome.

The specification discloses that neutralizing antibody titers can be achieved when a sheep fetus in the third trimester are inoculated with either inactivated BHV or a DNA plasmid comprising a DNA sequence encoding BHV antigen gD by injected of the virus or plasmid into the oral cavity of the sheep fetus in utero. The four sheep fetuses inoculated with BHV-1 gD DNA sequences are disclosed as each developing high titers of gD-specific titers. The BHV-1 inoculated fetus developed moderate gD specific antibody titers (see specification, pages 34 and 38). In addition, the fetal sheep were shown to develop cell immune responses as demonstrated by lymphoproliferative response assays (specification, page 39). Further, the specification discloses that booster immunizations with gD DNA sequences enhanced the immune response achieved in fetal immunized sheep (specification, page 40). However, there is no evidence that the antibody titers or cellular responses achieved were predictive of protection against an HBV-1 challenge.

One critical parameter to the claimed invention would be the time of administration of the nucleic acid sequence encoding an antigen. During fetal development, a situation referred as "self tolerance" or "self-recognition" arises. This is where the immature immune system of the fetus begins to recognize the cells,

tissues and organs of the fetus as "self" that is that the immune system will not attack the cells, organs or tissues of the fetus. Should an antigen be administered to a fetus prior to the establishment of self-recognition, the fetus' immune system would recognize the antigen as abnormal constituent of the developing fetus and thus not recognize the antigen as foreign when challenged. In this situation, there would be no protection against an infective agent, pathogen or other invading protein. The specification discloses that administration of the DNA sequence in the third trimester, days 123 and 124 of a 148-day gestation, resulted in the formation of neutralizing antibodies. Thus, the specification only enables the administration of the DNA sequence late in pregnancy. Further, the specific examples are sheep. There is no discussion or suggestion for the administration of a DNA vaccine to other mammals, or vertebrates, such that an immune response would be achieved as a result of a challenge subsequent to inoculation.

Another issue concerning the present is disclosure is the extent to which an immune response in fetal sheep would be seen as predictive of a similar immune response in other mammals, or vertebrates. Watts et al state that a baboon model was used to study the inoculation of a hepatitis B virus subunit vaccine because the baboon is immunologically similar to humans and that baboon represents an animal model of maternal and fetal vaccination comparable to humans (Watts, page 427, col. 2, parag. 1, lines 5—9). Thus, the sheep model disclosed does not appear to be regarded by the art as being relevant to human vaccination, and its relevance to the vaccination in other mammals is not clear.

In addition, there is no evidence that the claimed invention would be enabled for its full breadth. For example, RNA viruses, such HIV and rhinoviruses, are well known in the art to have evaded vaccination protocols primarily because their antigens mutate to change amino acid sequence. Thus, a DNA sequence encoding a

viral vaccine would have a similar problem with induction of a protective immune response because the DNA sequence would encode the mutated protein. Thus, there is no evidence of record that the claimed method would be enabled for the breadth of the claimed invention.

Thus, at the time of the present invention, the skilled artisan would have been required to undertake an undue amount of experimentation without a predictable degree of success to implement the invention as claimed.

The claims are free of the prior art. At the time of filing, the prior art did not teach or suggest methods of eliciting an immune response in a vertebrate subject comprising administering a vaccine composition mucosally to the subject in utero comprising a nucleic a molecule encoding an antigen or methods of eliciting an immune response in a vertebrate subject comprising administering to a mucosal membrane of a vertebrate in utero during the third trimester a first vaccine composition comprising a nucleic acid molecule encoding and antigen, and administering the first vaccine composition a second time to the vertebrate at birth.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0408. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

August 5, 2004